REMARKS

The Examiner has required restriction in the above-identified application as follows:

Group I: Claims 1-54, drawn to adenovirus vectors comprising a target cell specific TRE; and

Group II: Claims 55-58, drawn to a method of propagation of a replication competent adenovirus vector comprising a target specific TRE and first and second genes cotranscribed using an IRES and a method of modifying the genotype of a cell or selective cytotoxicity of a cell.

Applicant respectfully submits that examination of all currently pending claims would not pose an undue burden on the Examiner. Section 803 of The Manual of Patent Examining Procedure states that "[i]f the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions." Applicant therefore respectfully requests examination of all currently pending claims.

The above amendments are being made to more clearly define the Applicants' invention. Upon entry of the foregoing amendment, Claims 59-88 will remain pending in the application. Claims 1-58 have been canceled. No new matter has been introduced and entry is respectfully requested. Support for the claims can be found in the specification at least in the following locations:

Claim 59 finds support in the specification as filed at least on page 10, lines 21-23 (a replication-competent adenoviral vector for selective cytotoxicity of a target cell); page 8, lines 2-9 (comprising first and second co-transcribed genes wherein the first and second genes are under transcriptional control of a heterologous, target cell-specific TRE); page 14, lines 16-20 and 26-28 (the second gene has a mutation in or deletion of its endogenous promoter and is under

translational control of an internal ribosome entry site or IRES).

Claim 60 which states that the adenoviral gene essential for replication is an early gene selected from the group consisting of E1A, E1B, E2 and E4 finds support in the specification as filed at least on page 8, lines 10-13;

Claim 61 which states that the adenoviral gene essential for replication is a late gene finds support in the specification as filed at least on page 8, lines 10-13;

Claims 62-66, which recite particular TREs, including a prostate antigen specific TRE (PSA-TRE), a glandular kallikrein TRE (hk-TRE), a probasin (PB-TRE), an alpha-fetoprotein TRE (AFP-TRE), a carcinoembryonic antigen TRE (CEA-TRE), a cell status TRE, a melanocyte cell-specific TRE, a mucin (MUC1) TRE, and a uroplakin TRE (UP-TRE) find support in the specification as filed at least on page 9, lines 14-22 and from page 23, line 1 through page 25, line 18;

Claims 67 and 68, which recite an HSV-tk and/or cytosine deaminase (cd) gene find support in the specification as filed at least on page 72, lines 20-23;

Claims 69 and 70, which recite cytokine genes, in particular, GM-CSF, find support in the specification as filed at least on page 73, lines 9-13.

Claims 67 and 71, which recite a gene encoding a factor capable of initiating apoptosis, in particular a Fas gene find support in the specification as filed at least on page 72, lines 25-page 73, line 9.

Claims 67, 72 and 73, which recite reporter genes, in particular, reporter genes selected from the group consisting of lacZ gene, luciferase, alkaline phosphatase and green fluorescent protein find support in the specification as filed at least on page 71, lines 23 through page 72, line 2.

Claim 74 which states that said first gene has a mutation in or deletion of its endogenous

promoter finds support in the specification as filed at least on page 68, lines 19-22.

Claim 75 which states that said first gene has a deletion or inactivation of an enhancer region finds support in the specification as filed at least on page 9, lines 7-8.

Claim76 which states that said first gene is an E1A gene and the endogenous E1A promoter is mutated or deleted finds support in the specification as filed at least on page 8, lines 17-20 and 25-27.

Claim 77 which states that said first gene is an E1A gene and the endogenous E1A enhancer I is mutated or deleted finds support in the specification as filed at least on page 9, lines 7-9.

Claim 78 which states that said first gene is an E1B gene and the endogenous E1B promoter is mutated or deleted finds support in the specification as filed at least on page 8, line 27 through page 9, line 2.

Claim 79 which states that said E1B gene has a deletion in or mutation of the 19-kDa region finds support in the specification as filed at least on page 9, lines 3-6 and on page 25, lines 19-27.

Claims 80 and 81, which state that said adenovirus comprises an E3 region or portion thereof find support in the specification as filed at least in Fig. 6 on page 29, lines 13-21 and on page 69, line 25 through page 70, line 26.

Claim 82 which states that said IRES is from EMCV finds support in the specification as filed at least on page 19, lines 14-16.

Claim 83 which states that said IRES is from VEGF finds support in the specification as filed at least on page 19, lines 16-17.

Claims 84 and 85, which recite a composition comprising an adenoviral vector and a pharmaceutically acceptable excipient find support in the specification as filed at least on page

10, lines 8-9.

Claims 86 and 87, which recite an isolated host cell comprising an adenoviral vector find support in the specification as filed at least on page 10, lines 12-14.

Claim 88 which recites a method for ex vivo propagation of an adenoviral vector of Claim 59 finds support in the specification as filed at least on page 10, lines 15-20.

CONCLUSION

This application is now in condition for examination on the merits. Favorable consideration is respectfully requested. If, however, any points remain in issue which the Examiner feels may be best resolved through a personal or telephonic interview, the Examiner is respectfully requested to contact Linda. R. Judge at (415) 836-2586.

Respectfully submitted,

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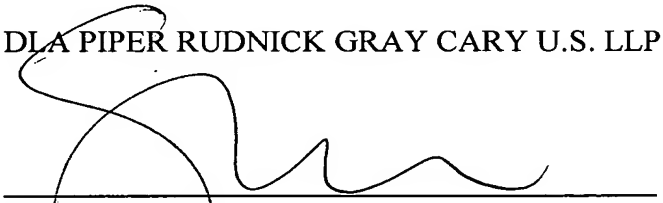

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